We Claim:

1. A method of non-invasive immunization in an animal and/or a method of inducing a systemic immune response or systemic therapeutic response to a gene product, in an animal, comprising contacting skin of the animal with a vector chosen from the group of bacterial vectors, baculovirus vectors, yeast vectors and vertebrate tissue culture cells, wherein the vector comprises and expresses a nucleic acid molecule encoding the gene product, in an amount effective to induce the response.

2. The method of claim1, wherein the vector is an *Escherichia* bacterial vector.

3. The method of claim 2 wherein the *Escherichia* vector is *Escherichia coli.*

4. The method of claim 1 wherein the nucleic acid molecule is exogenous or heterologous to the vector.

5. The method of claim 1 wherein the response comprises a systemic immune response.

6. The method of claim 1 wherein the vector comprises and expresses an exogenous nucleic acid molecule encoding an epitope of interest.

7. The method of claim 1 wherein the vector comprises and expresses an antigen.

8. The method of claim 1 wherein the vector comprises and expresses a therapeutic product.

9. The method of claim 1 wherein the nucleic acid molecule encodes an epitope of interest and/or an antigen of interest and/or a nucleic acid molecule that stimulates and/or modulates an immunological response and/or stimulates and/or modulates expression comprising transcription and/or translation of an endogenous and/or exogenous nucleic acid molecule.

10. The method of claim 4 wherein the exogenous nucleic acid molecule encodes one or more of an antigen or portion thereof, or one or more of an epitope of interest, from a pathogen.

11. The method of claim 4 wherein the exogenous nucleic acid molecule encodes one or more of: influenza hemagglutinin, influenza nuclear protein, influenza M2, tetanus toxin C-fragment, anthrax protective antigen, anthrax lethal factor, rabies glycoprotein, HBV surface antigen, HIV gp 120, HIV gp 160, human carcinoembryonic antigen, malaria CSP, malaria SSP, malaria MSP, malaria pfg, and mycobacterium tuberculosis HSP.

12. The method of claim 4 wherein the exogenous nucleic acid molecule encodes an immunomodulator.

13. The method of claim 1 wherein the response is induced by the vector expressing the nucleic acid molecule in the animal's cells.

14. The method of claim 13 wherein the cells comprise epidermal cells.

15. The method of claim 1 wherein the response is induced by the antigen expressed from the nucleic acid molecule within the bacterial vector.

16. The method of claim 1 wherein the response comprises an immune response against a pathogen or a neoplasm.

17. The method of claim 1 wherein the animal is a mammal.

18. The method of claim 17 wherein the mammal is a human or a companion or domesticated or food-or feed-producing or livestock or game or racing or sport animal.

19. The method of claim 18 wherein the animal is a cow, a horse, a dog, a cat, a goat, a sheep, or a pig.

20. The method of claim 1 wherein the bacterium comprises an exogenous or heterologous nucleic acid molecule encoding the gene product for the response.

21. The method of claim 20 wherein the nucleic acid molecule is exogenous or heterologous and encodes an epitope of interest and the method is for inducing a systemic immunological response.

22. The method of claim 21 wherein the nucleic acid molecule is exogenous or heterologous and encodes one or more influenza epitopes of interest and/or one or more influenza antigens.

23. The method of claim 1 wherein the vector is matched to, or a natural pathogen of the animal.

24. The method of claim 1 comprising application of a delivery device including the vector to the skin of the animal.

25. The method of claim 24 further comprising disposing the vector in and/or on the delivery device.

26. The method of claim 25 further comprising at least one application of the delivery device including the vector to the skin of the animal.

27. The method of claim 26 further comprising multiple applications of the delivery device including the vector to the skin of the animal.

28. The method of claim 1 wherein the vector induces an anti-tumor effect in the animal by expressing an oncogene, a tumor-suppressor gene, or a tumor-associated gene.

29. The method of claim 12, wherein the immunomodulator comprises a co-stimulator and/or a cytokine.

30. The method of claim 4 wherein the response is against *Clostridium tetanus* infection.

31. The method of claim 4 wherein the exogenous nucleic acid molecule encodes tetanus toxin C-fragment.

32. The method of claim 4 wherein the exogenous nucleic acid molecule encodes an antigen or epitope of tetanus toxin.

33. The method of claim 24 wherein the hair is not removed from the skin prior to applying the delivery device to the skin of the animal.

34. The method of claim 24 wherein the hair is removed from the skin prior to applying the delivery device to the skin of the animal.

We Claim:

1. A method of non-invasive immunization in an animal and/or a method of inducing a systemic immune response or systemic therapeutic response to a gene product, in an animal, comprising contacting skin of the animal with a non-replicative vector chosen from the group of bacterium, virus, and fungus, wherein the vector comprises and expresses a nucleic acid molecule encoding the gene product, in an amount effective to induce the response.

2. The method of claim 1, wherein the vector is selected from *Clostridium tetani*, *Clostridium botulinum*, *Clostridium butyricum*, *Clostridium baratii*, *Escherichia coli*, *Salmonella typhimurium*, *Bacillus anthracis*, influenza virus, and yeasts that are rendered non-replicative by irradiation, antibiotics, fixatives, or gentle heat.

3. The method of claim 2, wherein the vector is rendered non-replicative by γ-irradiation.

4. The method of claim 1, wherein the gene products are botulinum neurotoxins, insulin, erythropoietin, tetanus toxin C-fragment, and growth hormone.

5. The method of claim 1 wherein the non-replicative vector is an *Escherichia* vector.

6. The method of claim 5 wherein the *Escherichia* vector is *Escherichia coli*.

7. The method of claim 1 wherein the nucleic acid molecule is exogenous or heterologous to the vector.

8. The method of claim 1 wherein the response comprises a systemic immune response.

9. The method of claim 1 wherein the vector comprises and expresses an exogenous nucleic acid molecule encoding an epitope of interest.

10. The method of claim 1 wherein the vector comprises and expresses an antigen.

11. The method of claim 1 wherein the vector comprises and expresses a therapeutic product.

12. The method of claim 1 wherein the nucleic acid molecule encodes an epitope of interest and/or an antigen of interest and/or a nucleic acid molecule that stimulates and/or modulates an immunological response and/or stimulates and/or modulates expression comprising transcription and/or translation of an endogenous and/or exogenous nucleic acid molecule.

13. The method of claim 7 wherein the exogenous nucleic acid molecule encodes one or more of an antigen or portion thereof, or one or more of an epitope of interest, from a pathogen.

14. The method of claim 7 wherein the exogenous nucleic acid molecule encodes one or

more of: influenza hemagglutinin, influenza nuclear protein, influenza M2, tetanus toxin C-fragment, anthrax protective antigen, anthrax lethal factor, anthrax germination factors, rabies glycoprotein, HBV surface antigen, HIV gp120, HIV gp160, human carcinoembryonic antigen, malaria CSP, malaria SSP, malaria MSP, malaria pfg, botulinum toxin A, and mycobacterium tuberculosis HSP.

15. The method of claim 7 wherein the exogenous nucleic acid molecule encodes an immunomodulator.

16. The method of claim 1 wherein the response is induced by the vector expressing the nucleic acid molecule in the animal's cells.

17. The method of claim 16 wherein the cells comprise epidermal cells.

18. The method of claim 1 wherein the response comprises an immune response against a pathogen or a neoplasm.

19. The method of claim 1 wherein the animal is a vertebrate.

20. The method of claim 19 wherein the vertebrate is a bird or mammal.

21. The method of claim 20 wherein the bird or mammal is a human or a companion or domesticated or food-or feed-producing or livestock or game or racing or sport animal.

22. The method of claim 21 wherein the animal is a cow, a horse, a dog, a cat, a goat, a sheep, a pig, or a chicken, or a duck, or a turkey.

23. The method of claim 1 wherein the bacterium comprises an exogenous or heterologous nucleic acid molecule encoding the gene product for the response.

24. The method of claim 23 wherein the nucleic acid molecule is exogenous or heterologous and encodes an epitope of interest and the method is for inducing a systemic immunological response.

25. The method of claim 24 wherein the nucleic acid molecule is exogenous or heterologous and encodes one or more tetanus and anthrax epitopes of interest and/or one or more influenza antigens.

26. The method of claim 1 wherein the vector is matched to, or a natural pathogen of, the animal.

27. The method of claim 1 comprising application of a delivery device including the vector to the skin of the animal.

28. The method of claim 27 further comprising disposing the vector in and/or on the delivery device.

29. The method of claim 28 further comprising at least one application of the delivery device including the vector to the skin of the animal.

30. The method of claim 29 further comprising multiple applications of the delivery device including the vector to the skin of the animal.

31. The method of claim 1 wherein the vector induces an anti-tumor effect in the animal by expressing an oncogene, a tumor-suppressor gene, or a tumor-associated gene.

32. The method of claim 15, wherein the immunomodulator comprises a co-stimulator and/or a cytokine.

33. The method of claim 7 wherein the response is against *Clostridium tetani* infection.

34. The method of claim 7 wherein the exogenous nucleic acid molecule encodes tetanus toxin C-fragment.

35. The method of claim 7 wherein the exogenous nucleic acid molecule encodes an antigen or epitope of tetanus toxin.

36. The method of claim 23 wherein the hair is not removed from the skin prior to applying the delivery device to the skin of the animal.

37. The method of claim 23 wherein the hair is removed from the skin prior to applying the delivery device to the skin of the animal.

38. The method of claim 14 wherein the exogenous nucleic acid encodes botulinum toxin A.

39. The method of claim 38, wherein the systemic therapeutic response is used in cosmetic treatments or in the treatment of neuromuscular disorders characterized by hyperactive skeletal muscles.

40. The method of claim 39, wherein the cosmetic treatments include the reduction of facial or neck wrinkles.

41. The method of claim 40, wherein the facial wrinkles are glabellar lines.

42. The method of claim 39, wherein the neuromuscular disorder is selected from the group consisting of: migraine headaches, blepharospasm, strabismus spasm, hemifacial spasm, spasmodic dysphonia, dystonias in general, hyperhidrosis, and cerebal palsy.

43. A method of non-invasive immunization in an animal and/or a method of inducing a

systemic immune response or systemic therapeutic response to a gene product, in an animal, comprising contacting skin of the animal with cell-free extracts in an amount effective to induce the response, wherein the extracts are prepared by filtration of disrupted cells or vectors, wherein the cell or vector comprises and expresses a nucleic acid molecule encoding the gene product.

44. The method of claim 43, wherein the cells or vectors are selected from the group consisting of bacterium, fungus, cultured animal cells and cultured plant cells.

45. The method of claim 43, wherein the cells are disrupted by sonication.

46. The method of claim 45, wherein the cells are not lysed by the sonication.

47. The method of claim 46, wherein the cells remain viable after the sonication.

48. The method of claim 45, wherein the cells are sonicated at a frequency of 20 kHz.

49. The method of claim 45, wherein the sonication results in cavitation.

50. The method of claim 45, wherein the sonication comprises fewer than 240 cycles, wherein each cycle comprises 15 seconds of sonication followed by 1 minute of no sonication.

51. The method of claim 45, wherein the sonication comprises fewer than 240 cycles, wherein each cycle comprises 15 seconds of sonication followed by 1 minute of no sonication.

52. The method of claim 51, wherein the sonication comprises fewer than 200 cycles.

53. The method of claim 52, wherein the sonication comprises fewer than 150 cycles.

54. The method of claim 53, wherein the sonication comprises fewer than 100 cycles.

55. The method of claim 54, wherein the sonication comprises fewer than 75 cycles.

56. The method of claim 55, wherein the sonication comprises fewer than 50 cycles.

57. The method of claim 56, wherein the sonication comprises fewer than 40 cycles.

58. The method of claim 57, wherein the sonication comprises fewer than 30 cycles.

59. The method of claim 58, wherein the sonication comprises fewer than 20 cycles.

60. The method of claim 59, wherein the sonication comprises 20 cycles.

61. The method of claim 44 wherein the cell is a bacterium.

62. The method of claim 61, wherein the bacterium is selected from *Clostridium*, *Escherichia*, *Salmonella*, and *Bacillus*.

63. The method of claim 62, wherein the bacterium is an *Escherichia*.

64. The method of claim 63, wherein the bacterium is *Escherichia coli*.

65. The method of claim 43, wherein the gene products are botulinum neurotoxins, insulin,

erythropoietin, tetanus toxin C-fragment, and growth hormone.

66. The method of claim 65, wherein the nucleic acid molecule is exogenous or heterologous to the vector.

67. The method of claim 43, wherein the response comprises a systemic immune response.

68. The method of claim 43, wherein the cell comprises and expresses an antigen.

69. The method of claim 43, wherein the cell comprises and expresses a therapeutic product.

70. The method of claim 43, wherein the nucleic acid molecule encodes an epitope of interest and/or an antigen of interest and/or a nucleic acid molecule that stimulates and/or modulates an immunological response and/or stimulates and/or modulates expression comprising transcription and/or translation of an endogenous and/or exogenous nucleic acid molecule.

71. The method of claim 66, wherein the exogenous nucleic acid molecule encodes one or more of an antigen or portion thereof, or one or more of an epitope of interest, from a pathogen.

72. The method of claim 66, wherein the exogenous nucleic acid molecule encodes one or more of: influenza hemagglutinin, influenza nuclear protein, influenza M2, tetanus toxin C-fragment, anthrax protective antigen, anthrax lethal factor, anthrax germination factors, rabies glycoprotein, HBV surface antigen, HIV gp120, HIV gp160, human carcinoembryonic antigen, malaria CSP, malaria SSP, malaria MSP, malaria pfg, botulinum toxin A, and mycobacterium tuberculosis HSP.

73. The method of claim 66, wherein the exogenous nucleic acid molecule encodes an immunomodulator.

74. The method of claim 43, wherein the response comprises an immune response against a pathogen or a neoplasm.

75. The method of claim 43 wherein the animal is a vertebrate.

76. The method of claim 75 wherein the vertebrate is a bird or mammal.

77. The method of claim 76 wherein the bird or mammal is a human or a companion or domesticated or food- or feed-producing or livestock or game or racing or sport animal.

78. The method of claim 43 wherein the cell free extract contains the gene product.

79. The method of claim 43 comprising application of a delivery device including the extract to the skin of the animal.

80. The method of claim 79, further comprising disposing the extract in and/or on the delivery device.

81. The method of claim 80, further comprising at least one application of the delivery device including the extract to the skin of the animal.

82. The method of claim 81, further comprising multiple applications of the delivery device including the extract to the skin of the animal.

83. The method of claim 79, wherein the hair is not removed from the skin prior to applying the delivery device to the skin of the animal.

84. The method of claim 79, wherein the hair is removed from the skin prior to applying the delivery device to the skin of the animal.

85. A method of enhancing the immunogenicity and efficacy of an epicutaneous vaccine for inducing a systemic immune response to an antigen, in an animal, comprising contacting skin of the animal with a vaccine admixed with heat-shock protein 27, in an amount effective to induce the response.

86. The method of claim 85, wherein the vaccines are vector-, nucleic acid-, or protein-based vaccines.

87. The method of claim 1, further comprising admixing the non-replicative vector with heat-shock protein 27 prior to contacting the skin of the animal.

88. The method of claim 43, further comprising admixing the cell-free extract with heat shock protein 27 prior to contacting the skin of the animal.

89. The method of claim 43, further comprising admixing the cells with heat shock protein 27 prior to disruption of the cell.

90. The method of claim 87, wherein the immunization or immune response or system therapeutic response is enhanced.

91. The method of claim 88, wherein the immunization or immune response or system therapeutic response is enhanced.

92. The method of claim 89, wherein the immunization or immune response or system therapeutic response is enhanced.